REMARKS

Status of the Claims

Claims 5, 6 and 20 were pending as shown in the Request to Reopen Prosecution under 37 C.F.R. § 41.50 following the Board of Patent Appeals reversal of the Examiner's rejection in Appeal No. 2006-3085, Decision mailed May 30, 2007. By amendment herein, new claim 21 has been added. Support for new claim 21 is found, for example, on page 11, lines 20-21 and Fig. 4A. Thus, claims 5, 6, 20 and 21 are pending as shown above.

35 U.S.C. 103

The rejection of previously pending claims 5, 6 and 20 under 35 U.S.C. § 103(a) as allegedly obvious over Pomerantz (1988) *Biochemistry* 37(4):965-970 (hereinafter "Pomerantz") in view of Krylov et al. (1994) *EMBO J.* 13(12):2849-2861 (hereinafter "Krylov") was reiterated by the Examiner. See, Office Action, pages 2-4 and Board Decision on Appeal, pages 12-15. Pomerantz was cited for disclosing a zinc finger protein fused to a naturally occurring dimerization domain extracted from the GAL4 protein and for suggesting the use of non-naturally occurring dimerization domains. *Id.* Krylov, reference 19 of Pomerantz, was cited for demonstrating that non-naturally occurring peptide linkers could be utilized to complex zinc finger proteins. *Id.*

Following the Decision on Appeal, Applicants filed a request to reopen prosecution and amended claim 5. Accordingly, the pending claims are drawn to a complex comprising two fusion proteins. Each fusion protein comprises a zinc finger protein and a non-naturally occurring peptide linker that forms a dimer with the corresponding non-naturally occurring peptide linker on a separate fusion protein. In addition, each zinc finger protein binds to DNA in a sequence-specific manner.

As acknowledged by the Office, Pomerantz does not teach or suggest non-naturally occurring linker peptides that dimerize with each other.

Furthermore, the citation in Pomerantz to Krylov does not cure the deficiency of Pomerantz because Krylov fails entirely to teach or suggest anything about zinc finger proteins complexed together via non-naturally occurring peptides fused to each of the zinc finger proteins. Rather, Krylov discloses only that certain amino acid residues that are part of naturally

occurring leucine zipper proteins can be mutated to modulate dimerization stability and specificity. Clearly, Krylov's dimerization mutants are not complexes of zinc finger proteins as claimed. Moreover, Krylov mutates residues in the context of a single naturally occurring protein, and, accordingly, this reference does not teach or suggest complexes in which each component of the complex is a fusion of a zinc finger protein and a non-naturally occurring linker.

Thus, because Pomerantz fails to teach fusions of zinc finger proteins and non-naturally occurring peptides that dimerize to join the zinc finger proteins and because Krylov fails to teach or suggest that the mutated leucine zipper dimerization domains are functional outside the context of their naturally occurring leucine zipper proteins, the references do not teach or suggest all the elements as claimed.

The rejection is also untenable because Krylov teaches away from using their mutant dimerizing outside of the context of a leucine zipper-containing protein (Krylov, page 2850, left column):

> These results produce protein design rules that can be used to modify leucine zipper-containing proteins.

Indeed, Krylov clearly teaches away from combining mutant leucine zipper dimerization domains with heterologous zinc finger domains because this reference clearly states that the whole leucine zipper protein is involved in the specificity of dimerization (Krylov, page 2859, left column):

> Since the specificity of dimerization is distributed throughout the length of the leucine zipper, the potential for modulation of dimerization partners is great.

Thus, Krylov teaches that the importance of overall interactions of the leucine zipper protein. As such, the skilled artisan reading Krylov would have no reason to isolate mutated dimerization domains from leucine zipper proteins, let alone use such isolated non-naturally occurring dimerization domains to replace Pomerantz's naturally occurring Gal4 dimerization domain to dimerize zinc finger proteins, as claimed.

The obviousness rejection is also untenable because modifying Krylov as suggested would destroy the intended function of the reference's proteins. As set forth by the Supreme

Court in *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. ___, 127 S. Ct. 1727 (2007) and Patent Office Guidelines regarding determining obviousness, an obviousness rejection is only proper when the proposed combination of elements can be made without changing the function of the structure or method disclosed in the references (see, Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in view of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Fed. Reg. Vol. 72, No. 195, October 10, 2007):

> The rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one or ordinary skill in the art at the time of the invention.

Thus, it is axiomatic that an obviousness rejection is improper where the proposed modification would destroy the intended function of the reference (see, e.g. *In re Fritch* 23 USPQ2d 1780, 1783, n.12 (Fed. Cir. 1992) and *In re Ratti* 123 USPQ 349, 352 (CCPA 1979)):

> A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose.
>
> [I]t would require a substantial reconstruction and redesign of the elements shown in [a cited reference] as well as a change in the basic principles under which [that reference's] construction was designed to operate.

In the case at hand, Krylov does not show that the mutant leucine zipper dimerization domains work when fused to a zinc finger domain. Indeed, given Krylov's teachings regarding the importance of entire leucine zipper protein in dimerization, it is plain that using non-naturally peptide linkers that dimerize fused to zinc finger domains as claimed would render Krylov's mutant dimerization domains inoperable for their intended purpose of dimerizing leucine zipper proteins. Since the proposed modifications would destroy the intended function of Krylov, there is no combination of Pomerantz and Krylov that renders the pending claims obvious.

For all of the aforementioned reasons, the rejection of claims 5, 6 and 20 under 35 U.S.C. § 103(a) should be withdrawn.

35 U.S.C. 102

Claims 5 and 6 were newly rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,242,568 (hereinafter "Barbas") or U.S. Patent No. 6,453,242 (hereinafter "Eisenberg"). (Office Action, pages 11-12). These rejections were not raised by the Board.

As noted in the Board's Decision on Appeal, anticipation requires a showing that each element of the claim is identifiable in a single reference. Board Decision, page 12, citing *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 77 USPQ2d 1321, 1325 (Fed. Cir. 2005).

In the instant case, Barbas does not disclose complexes as claimed. Barbas fails to disclose non-naturally occurring linkers, disclosing instead only the naturally occurring Fos/Jun dimerization domains (col. 28, lines 27-30 of Barbas):

> Zinc finger proteins containing from about 2 to 20 zinc fingers Zif(2) to Zif(2), and preferably from about 2 to 12 zinc fingers, may be fused to leucine zipper domains of the Jun/Fos proteins ...

Furthermore, in terms of dimerization domains other Fos/Jun, Barbas does not teach non-naturally occurring peptides and, moreover, teaches that domains other than Fos/Jun are used to link a zinc finger protein to a different protein, which is unlike the claimed complexes of 2 zinc finger proteins (Barbas, col. 28, lines 31-34, emphasis added).

> Alternatively, zinc finger proteins **can be fused to other proteins which are capable of forming heterodimers and contain dimerization domains**. ...

Thus, Barbas fails to disclose all the elements of the claimed complexes and cannot anticipate claims 5 and 6.

Similarly, Eisenberg does not disclose complexes as set forth in claims 5 and 6. Eisenberg describes linking of zinc finger proteins via a single peptide linker that joins the zinc fingers to each other. This single linker does not specifically bind to a second linker in order to join the zinc finger proteins together. Thus, Eisenberg does not disclose all the elements of the claimed complexes.

For all of the aforementioned reasons, the rejections of claims 5 and 6 under 35 U.S.C. § 103(e) should be withdrawn.

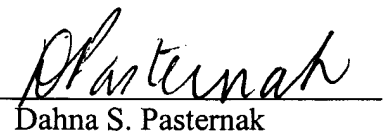
CONCLUSION

Applicants believe that the claimed subject matter is now in condition for allowance and early notification to that effect is respectfully requested. If any issues remain to be addressed, the Examiner is encouraged to telephone the undersigned.

Please address all correspondence to the undersigned.

Respectfully submitted,

Date: December 13, 2007

By: 

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